Identifying reproducible brain signatures of obsessive-compulsive profiles

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Primary Objective: To identify reproducible neuroimaging signatures of OCDSecondary Objective: To link these neuroimaging signatures to specific cognitive functions and clinical profilesExploratory Aims: 1) To study how environmental factors may…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Anxiety disorders and symptoms
Study type	Observational non invasive

Summary

ID

NL-OMON47923

Source
ToetsingOnline

Brief title
Brain signatures of OCD profiles

Condition

- Anxiety disorders and symptoms

Synonym
anxiety, neurosis, obsessive-compulsive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: National Institute of Mental Health (NIMH)

Intervention

Keyword: clinical profiles, cognitive profiles, magnetic resonance imaging, obsessive-compulsive disorder

Outcome measures

Primary outcome

1. clinical measures (on specific symptoms)

2. neurocognitive profiles (behaviour on neuropsychological tests)

3. neural correlates on regional brain volumes (e.g. cortical thickness,

surface area), white matter integrity (e.g. fractional anisotrophy), and

resting state network connectivity, using magnetic resonance imaging (MRI).

Secondary outcome

We will explore whether three factors (childhood trauma, socioeconomic status

(SES), and religiosity) moderate the link between our neuroimaging signatures

and clinical and cognitive profiles. We focus on childhood trauma and SES

because of their known effects on brain structure in healthy people, and their

potential to confound imaging data.

Study description

Background summary

OCD contributes to the global burden of disease. This project seeks to identify reproducible brain signatures for OCD cognitive and clinical profiles, using methods that are applicable to populations around the globe.

The phenotype of OCD is similar around the globe, including both core behaviors (obsessions and compulsions) and individual variation (e.g., symptom dimensions, age of onset, comorbidity). This is one reason why OCD is an excellent test for identifying reproducible neuroimaging signatures that can be linked to different cognitive and clinical profiles.

Brain circuit abnormalities have been identified in OCD subjects. We propose to test their reproducibility in a large unmedicated sample and to validate them by linking them to specific cognitive and clinical profiles.

Study objective

Primary Objective: To identify reproducible neuroimaging signatures of OCD

Secondary Objective: To link these neuroimaging signatures to specific cognitive functions and clinical profiles

Exploratory Aims:

1) To study how environmental factors may moderate these brain-behavior associations.
2) To study which neural correlates are markers of vulnerability (present in both the OCD patients and their unaffected siblings), resilience (present in the unaffected siblings but not the OCD patients), and disease (present in OCD patients, but not the unaffected siblings)
3) To study the predictive value of neural correlates for naturalistic course of disease at 1 year follow-up.

Study design

This cross-sectional multi-center study will run for 5 years, using harmonized data collection across 5 sites worldwide. The design includes 3 domains of profile assessment:

1) Demographic and clinical profiles, including assessment of environmental factors
We will implement a standardized protocol at all sites to clinically assess subjects. We will assess patients in their primary language. The clinical protocol will include well-validated measures that have been used around the globe and that tap different symptom domains.

The clinical measures to assess include:
a) Obsessive-Compulsive Profiles
* Total Severity: Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)102
* Dimensional Yale-Brown Obsessive-Compulsive Scale (DY-BOCS)108
* Insight: Brown Assessment of Beliefs Scale (BABS)130
* Age of Onset: Structured Clinical Interview for DSM-5 (SCID)
* University of Sao Paulo Sensory Phenomenon Scale (USP-SPS)109
* Obsessive-Compulsive Personality Disorder (OCPD) assessment, based on SCID
b) Depression: Hamilton Depression Rating Scale (HAM-D)131
c) Anxiety: Hamilton Anxiety Rating Scale (HAM-A)132
d) Global Functioning: WHO Disability Assessment Schedule (WHODAS)134

e) History of Tic Disorders, using the structured interview (SCID)
f) Obsessive-Compulsive Inventory-Revised (OCI-R)
g) Autism: Autism Questionnaire (AQ)
h) Impulsivity: Impulsive-Compulsive Behaviors Checklist (ICBC)
i) Disgust: Disgust Propensity and Sensitivity Scale-Revised (DPSS-R)

2) Neuropsychological profiles
Neurocognitive tasks were chosen that: 1) probe the brain circuits and domains of cognitive dysfunction that are implicated in OCD; 2) are consonant with the NIMH*s RDoC matrix (http://www.nimh.nih.gov/research-priorities/rdoc/nimh-research-domain-criteria-rdoc.shtml); 3) can be standardized across sites (e.g., minimal reliance on language and computerized); and 4) are in the public domain (e.g., NIH toolkit, https://penncnp.med.upenn.edu, PhenXtoolkit).

These tasks will probe:
a) the dorsal *cognitive* CSTC circuit using the visual spatial N-BACK task to assess the executive function of updating and the Tower of London task to assess planning.
b) the ventral *cognitive* CSTC using the Stop-Signal Task to assess response inhibition.
c) the ventral *reward* CSTC using a Temporal Discounting and Risk and Choice task to assess capacity to delay reward, and the Habit task
d) the frontal-limbic circuitry using the Emotional Stroop task.
e) the sensorimotor CSTC using the Motor Sequence test.

3) Neural profiles
We will implement a standardized imaging protocol across all sites. At all sites, the MRI will be performed within one week of the clinical and neurocognitive assessments on a 3.0 Tesla whole-body scanner (GE MR750 [2 sites], Siemens Skyra [2 sites], and Philips Achieva [1 site]), all equipped with a 32 channel phased-array head coil. Images will be acquired with optimized and standardized sequences for:
a. high resolution 3D T1 weighted structural imaging with 1 mm isotropic resolution and additional phase-sensitive inversion recovery (psir) T1 weighted scan to optimize the segmentation in the subcortical areas
b. multi-shell diffusion tensor imaging (DTI) based on 73 high b-values: 25 in the first shell (b1000), and 24 in the 2 higher shells (b2000 and b3000) with 2,5 mm isotropic resolution, and 7 unweighted (b=0 s/mm2) scans
c. rs-fMRI (10 minutes, eyes closed): 272 volumes with 3.3 mm isotropic resolution.
Head motion will be monitored during scanning

At study start, we will harmonize data collection so that raw MRI data (anatomical, DTI and rs-fMRI) can be optimally pooled. We will follow

established methods used in other multi-center MRI studies to reduce between-scanner effects.

Study burden and risks

Participants will be measured at baseline during 3 assessment days (within a timeframe of max. two weeks) of 4 hours for clinical/neuropsychological assessments (psychiatric assessment (2 hours); self-report questionnaires (1 hour); neurocognitive assessment (2 hours)) and a 1 hour MRI scan session within one week of the clinical/neuropsychological assessments. 1 year follow-up session (Telephone) (0.5-1 hour)

There will be no direct benefit for the subjects to participate in the study. However, participation is expected to result in increased insight in to neurobiological background of the disorder, which will contribute subsequently to the development of treatment alternatives. The risks can be considered negligible. MRI is non-invasive imaging techniques. For subjects who are sensitive to claustrophobia, the positioning in a MRI scanner might provoke feelings of distress or in extreme situations panic attacks. In case a subject feels uncomfortable in the scanner, it is possible to terminate the scanning session at any moment without any consequence for the participant.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1) OCD patients (n <= 250):
* Either gender, all ethnic/racial-cultural categories, and right-handed (based on the Edinburgh Handedness Inventory);
* Ages 18- 50;
* Meets current DSM-5 criteria for OCD, with both obsessions and compulsions;
* OCD is the principal psychiatric problem and severity of illness is at least moderate (i.e., a Yale-Brown Obsessive Compulsive Scale (YBOCS) score of at least 16);
* Not on psychotropic medication (for at least 6 weeks; benzodiazepines / sleeping medication at least 1 week) and able to tolerate a treatment-free period;
* Capacity to provide informed consent;
* No current cognitive behavioral therapy (exposure in vivo with response prevention) for their OCD symptoms (last 6 weeks).;2) Healthy controls (n<=250):
* Either gender, all ethnic/racial-cultural categories;
* Ages 18-50;
* Capacity to provide informed consent.;3) Unaffected siblings (n<= 120-125):
* Either gender, all ethnic/racial-cultural categories;
* Ages 18-50;
* Capacity to provide informed consent;
* Sibling (first degree) of OCD participant.

Exclusion criteria

1) OCD patients:
* Lifetime diagnosis of a psychotic disorder, bipolar disorder, anorexia nervosa (note: binge eating and bulimia in past is OK, if not last 12 months), Tourette disorder or autism spectrum disorder with IQ < 80 (Asperger is OK, if OCD is primary);
* Current diagnosis (past 12 months) of any DSM-5 Substance-related and Addictive disorder (including nicotine) or chronic tic disorder, current diagnosis of Tourette Disorder. Note: Comorbid depressive or anxiety disorders and tics will be allowed if OCD is the principal diagnosis (i.e., most severe upon presentation and reason for seeking help).
* Active suicidal ideation;
* Females who are pregnant;
* Major medical or neurological problem (e.g., unstable hypertension, seizure disorder, head trauma (with loss of consciousness), neurocognitive disorder);
* Presence of metallic devices or dental braces (including retainers);

* IQ <80.;2) Healthy controls:
* Any current psychiatric diagnosis;
* Lifetime psychiatric diagnosis with the sole exception of major depressive disorder and anxiety disorders (Note: MDD and anxiety disorders OK only if not within the past 12 months);
* History and current use of psychotropic medication with the exception of sporadic sleeping drugs / benzodiazepines and only if not within the past week and not during study);
* OCD or tic disorder in a first- degree relative;
* Females who are pregnant;
* Major medical or neurological problem (e.g., unstable hypertension, seizure disorder, head trauma (with loss of consciousness));
* Presence of metallic devices or dental braces (including retainers with metal);
* IQ <80.;3) Unaffected siblings:
* Any current psychiatric diagnosis;
* Lifetime psychiatric diagnosis with the sole exception of major depressive disorder and anxiety disorders (Note: MDD and anxiety disorders OK only of not within the past 12 months);
* History and current use of psychotropic medication with the exception of sporadic sleeping drugs / benzodiazepines and only if not within the past week and not during study);
* Females who are pregnant;
* Major medical or neurological problem (e.g., unstable hypertension, seizure disorder, head trauma (with loss of consciousness));
* Presence of metallic devices or dental braces (including retainers with metal);
* IQ <80.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-01-2018
Enrollment:	125
Type:	Actual

Ethics review

Approved WMO Date:	19-07-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-02-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-08-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL61982.029.17